EXPERIMENTAL INOCULATION OF HUMANS WITH ECTODERMOTROPIC VIRUSES*

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Students of human infectious disease have a much greater opportunity to gain an understanding of pathogenesis when the disease can be experimentally reproduced in man at will. In this paper we shall describe our efforts to promote the inoculation of human skin with the following ectodermotropic viruses: the wart virus (verruca vulgaris and condyloma acuminatum), vaccinia, molluscum contagiosum, herpes simplex and herpes zoster. A review of previous attempts is appended.

METHODS

With the exception of the vaccinia virus, it is not at all easy to inoculate humans successfully with the above mentioned viruses. "Takes" are infrequent and erratic. Knowing that viruses multiply best in embryonic tissue, the assumption was made that regenerating epidermal cells after previous removal of the epidermis might in some respects be comparable to embryonic cells and provide a more favorable milieu for virus growth. The methods used for this purpose were: a) the dermabrasion technic, and b) the production of cantharidin blisters. The dermabrasion procedure is the one ordinarily used in removing acne scars in which the skin is first frozen with a refrigerant gas and then planed with a revolving wire brush or serrated stone. Cantharidin blisters were raised by introducing 0.25 ml of a 0.5% acetone solution of cantharidin into a glass cup about 1″ in diameter. The acetone was evaporated under a stream of air and the site covered with a gauze bandage. Inoculations were made into the prepared sites and symmetrical control sites at time intervals ranging from 3 days to 12 weeks. Healthy colored male volunteers, 20 to 45 years of age, inmates of the Philadelphia County Prison, served as subjects. We mostly used the volar surface of the forearm but in recognition of the great regional variations of the skin, other sites were also tested.

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Vaccinia

To test the hypothesis that freshly regenerated epidermis would promote virus infection, we did a pilot study with vaccinia in view of the ease of vaccination and the definite knowledge of its course. The vaccinations were carried out in the usual way (multiple puncture technic), using 106 adult subjects, all of whom had been previously vaccinated. The anticipated immune response was observed in every instance. In all, 312 inoculations were made, one forearm site serving as the control with the corresponding site on the opposite forearm having been prepared either by dermabrasion or by cantharidin. The inoculations were performed at intervals varying from 1 to 18 weeks after preparation. As a standard of comparison, the diameters of the lesions (exclusive of simple erythema) were measured on the third day post vaccination.

A condensation of the significant findings is given in Table I. To show best the enhancing effect of special preparation, the number and percentage of instances in which the reactions were at least twice the size of the control sites are recorded. The control sites ranged in diameter from 0.5–1.5 cm. In the prepared sites the range was 0.5 to 10.0 cm. The reactions in the dermabrasion sites were consistently larger than in cantharidin sites. With the former technique, 73% of 87 tests gave reactions at least twice as great as the control sites whereas the corresponding figure for the cantharidin site is 36% of 88 tests. It will be seen that the size of the reaction is highly dependent on the time interval after preparation of the site. With the dermabrasion technic, the optimal time for the maximum lesion was one month after preparation. At that time all the inoculations yield lesions at least twice the size of the controls. Indeed, the reactions averaged five times the size of the controls. Inoculations performed less than 6 days after dermabrasion uniformly failed. In sharp contrast to this, the optimal time with the cantharidin technic, was one week, at which time 81% of the lesions were at least twice the size of the controls; however, average diameters were

TABLE I

Vaccinia Inoculations

Weeks	Dermabrasion		Cantharidin	
	Number of tests	Dermabrasion at least twice normal reaction	Number of tests	Cantharidin at least twice normal reaction
1	15	9 (60%)	16	13 (81%)
2	12	6 (50%)	12	4 (33%)
3	19	15 (79%)	18	5 (28%)
4	11	11 (100%)	11	2 (18%)
5	12	8 (66%)	12	2 (20%)
6	7	6 (86%)	7	1 (14%)
7	—	—	—	—
8	2	2 (100%)	2	2 (100%)
9	4	3 (75%)	5	2 (40%)
10	—	—	—	—
11		—	—	—
12	2	2	2	1
13	1	1	1	0
14	—	—	—	—
15	—	—	—	—
16	—	—	—	—
17	—	—	—	—
18	2	1	2	0
Average:	87	64 (73%)	88	32 (36%)

usually 1–2 cm less than in dermabrasion sites. The dermabrasion technic clearly gave superior results by these standards. In accounting for these differences, it should be recognized that dermabrasion is a far more damaging procedure which completely removes the epidermis, whereas a layer of epidermal cells subtends the bullae produced by cantharidin and the inflammation is less intense. Perhaps an optimal period of 4 weeks with the dermabrasion technic as compared to one week with cantharidin indicates approximately similar stages of regeneration at these times.

Subsequent studies with other ectodermotropic viruses utilized these optimal times.

Molluscum contagiosum

The infectious nature of molluscum contagiosum has been suggested by many reports of accidental transmission of the disease by direct human contact. Attempts to induce molluscum lesions in laboratory animals have been unsuccessful.

Juliusberg (1) was the first (1905) to establish the viral nature of the causative agent experimentally. He ground the cores of molluscum lesions, suspended the material in broth and passed it through a Chamberland filter. The filtrate was inoculated into scarified areas of the upper arm of 3 individuals. After 50 days a papular lesion developed in one of the inoculated sites. A biopsy specimen of this lesion showed the typical histological structure of a molluscum lesion.

Wile and Kingery (2) repeated this experiment in 1919 with molluscum material passed through a Berkefeld filter and injected intracutaneously. Papules developed in the inoculation areas after 2–3 weeks and typical molluscum lesions were present by 8 weeks.

Findlay (3) repeated these experiments using molluscum material stored in 50% glycerol for 1 month.

Neither Pinkus (4) nor Blank and Rake (5) were able to induce experimental molluscum lesions.

Present study

Using 3 different sources (children under 10 years of age) cores of molluscum lesions were ground in 1 cc of normal saline and inoculated into scarified normal forearm skin and into sites prepared by dermabrasion and cantharidin. In addition, a number of inoculations were made into the axillae. A total of 141 inoculations (60 of them at prepared areas) were performed in 30 individuals. In no case did a typical molluscum lesion develop during an average observation period of 6 months.

Comment

Although we had no success, we were able to confirm the observation of Pinkus (4) who described a papular "immune" (tuberculin type) reaction after inoculation of molluscum material. Blank and Rake (5) noticed similar reactions. In 21 of 30 individuals we observed erythema, edema and marked induration developing in one or several of the inoculated areas, the maximum reaction occurring between the 3rd and 5th day and disappearing after 7 to 10 days. Almost all of these reactions occurred in normal skin areas and only very rarely in areas prepared by dermabrasion or cantharidin. The explanation given by Pinkus and Blank and Rake for these delayed tuberculin type responses seems very attractive. They occur in persons rendered hypersensitive by a previous inapparent infection. If this assumption is correct, the great majority of adult

persons have sustained inapparent primary infections; only a small fraction of the population ever develop clinically apparent molluscum lesions. Furthermore, it may well be that inapparent infections which render the host allergic may also render it immune. From the kind of data we have given, it is impossible to tell whether the failure to produce manifest molluscum lesions is due to a preexisting immunity or whether an actual infection occurred which was inapparent. One way to attack this problem is to find out if previously non-allergic subjects become hypersensitive after inoculation with live virus. Finally, it should be appreciated that other totally unknown forces may determine whether infection, apparent or inapparent, will occur. Unfortunately, we did not determine whether the "tuberculin" type response was purely allergic by using killed virus. If live virus is required, the reaction is truly one of immunity similar to the immune response in ordinary vaccination.

Verruca vulgaris

Although Variot inoculated warts from a child into adults as early as 1893, Jadassohn (6) was the first in 1896 to establish the infectious nature of warts beyond doubt. Using ground wart material from 4 different lesions (2 verrucae planae and 2 papillomatous warts) from children under 12 years of age, he performed 74 inoculations into normal skin areas of hands and arms of 6 individuals. After an incubation period of 2–3 months flat wart-like lesions developed in 31 inoculated sites. All of the 6 individuals developed at least one lesion, some of them several from one or different sources. All of the experimental warts developed on the hands, none on the arms.

Lanz (7) reported 2 positive inoculations with wart material with an incubation period of 6 weeks. The viral nature of warts was first proved by Ciuffo (8) in 1907. Using ground material suspended in normal saline from cornified flat warts of the hand of a young man, he inoculated the Berkefeld filtrate into a scarified area of the dorsum of his hand. After 5 months, small papules developed.

With the same technic, Serra (9) inoculated filtered material from a wart of the hand into normal skin areas on the wrist, scalp and sulcus coronarius of 5 individuals. After 5–6 months wartlike lesions developed in 2 of the 5 inoculations, both of them at the wrist. Inoculations of 5 individuals with material from a papillomatous wart of the scalp were unsuccessful.

In 1924 Serra repeated his experiments using a filtrate of papillomatous warts of the scalp and the suprapubic area. Six of 18 inoculations in 3 volunteers were positive, all of them occurring on the dorsum of the hand. Four of these positive inoculations were observed in the subject from whom the original material was taken. Inoculations of the skin of the penis and the scalp were negative.

Tuccio (10) induced warts in the second generation. He used ground material from verrucae filiformes of the beard area and inoculated scarified areas of the upper arm of 5 individuals under 18 years of age and of his own arm. Warts developed in 4 of these areas after 5–6 months. One of them was used to produce a second generation wart.

Wile and Kingery (11) used material from several warts, passed it through a Berkefeld filter and injected the filtrate intracutaneously into the dorsa of hands of 3 individuals. Wartlike lesions were observed after 4–6 months in all inoculation areas.

Unusually long incubation periods were observed by Ziegler (12). Warts were observed after 18 months in 4 of 6 inoculations of the arm.

Templeton (13) also observed long incubation periods. After intradermal inoculation of a wart filtrate, lesions developed in 2 out of 6 areas after a period of 12 and 20 months.

Kingery (14) produced second generation warts by inoculation of Berkefeld filtered wart material.

Ullmann (15) worked with material from larynx papillomas. Three of 4 inoculations with unfiltered material produced flat warts of the face and a papillomatous wart of the scalp after 2–3 months. He was able to repeat these inoculations successfully up to the third generation and noticed that the incubation period seemed to be shorter after repeated inoculations (from 2–4 months shortened to 4–5 weeks). With a bacteria free filtrate of larynx papillomas, he produced warts in 2 of 6 inoculations.

Lyell and Miles (16) differentiated 2 types of warts (banal or common warts and "myrmecia" or inclusion body warts) with different clinical and histological features. They inoculated 5 volunteers with a tissue extract from a banal wart and observed warts in 3 cases after 10–12

months. Inoculations with material from a myrmecia type wart into normal skin areas of 6 volunteers induced one myrmecia type wart after 5½ months.

Present study

One group of patients was inoculated with material from ordinary warts (verruca vulgaris) and another group with condyloma acuminatum.

(1) *Verruca vulgaris*

A suspension of freshly ground wart material in normal saline was inoculated into scarified normal and prepared (dermabrasion and cantharidin) skin areas of the arm. The areas were covered with moist filter paper and occluded under adhesive tape for one day. In addition, other skin areas, such as hands, face, back, scalp, axillae and sulcus coronarius penis were chosen for inoculation to test the influence of local factors. Although 6 different sources were used (papillomatous warts from the beard area and the nose of young adults) and a total of 159 inoculations (64 of them in prepared areas) were carried out in 36 different individuals, only one wart could be produced experimentally. The observation period was 6 to 18 months.

The source of the positive inoculation was a papillomatous wart from the beard area of a young colored male. The inoculation site was the forearm, 7 days after dermabrasion. After 3 months small pin point sized dark papules in linear arrangement were noticed. The lesions continued growing during the following weeks and formed a typical papillomatous wart, 1.5 cm in diameter and 0.8 cm elevated above the surrounding normal skin. The wart stopped growing after 6 weeks. Half of the lesion was excised for histopathologic examination. The remainder of the lesion disappeared spontaneously during the following 3 weeks.

(2) *Condyloma acuminatum*

Attempts to transmit warts and condylomata acuminata to laboratory animals have been unsuccessful. Negative results of inoculations with condyloma material into human skin have been reported by more than 10 authors. The first successful inoculation was performed by Waelsch (17) in 1917. At the same time he was the first to confirm the hypothesis that the same agent causes verruca vulgaris and condyloma acuminatum. Using ground unfiltered material from a penile condyloma lesion, he inoculated scarified skin areas of 3 volunteers. All 3 inoculations were successful; one flat wart developed on the forearm after 3 months and another on the forearm of another individual after 9 months. Inoculations into the labium minus produced typical condyloma lesions after 3 months.

The viral etiology of condylomata acuminata was established by Serra (18). He used material from penile condylomata of a patient who at the same time had papillomatous warts elsewhere. The condyloma material was filtered through a Chamberland filter and inoculated into 25 different scarified skin areas of 3 adult volunteers, (dorsum of the foot, labium majus, clitoris, perineum, suprapubic area, scalp, coronal sulcus and dorsum of hand). In 3 of 6 inoculated areas on the dorsum of the foot of one individual, 3 wartlike lesions developed after 5 months and 1 out of 10 inoculations into the suprapubic area developed a wart. None of the inoculations of the genital areas was successful.

Frey (19) produced a wart on the forearm 11 months after inoculation of condyloma material from the same patient.

Present study

Ground material from one fresh penile condyloma lesion was suspended in 1 cc of normal saline and inoculated into normal and specially prepared skin areas. The areas were covered with moist filterpaper and occlusive dressings for 1 day. 47 inoculations were performed in 7 volunteers into different skin areas (forearm, palm and dorsum of hand, back, face, scalp, axillae and the coronal sulcus of the penis). All of the recipients developed at least one lesion, some of them 2 lesions at different localizations. In all, 10 of 47 inoculations were successful. Wartlike lesions were observed on 3 unprepared normal areas of the forearm, 3 on the upper back and 4 in the axillae. No takes occurred on the hands, scalp, face and penis. The incubation time was 6, 6 and 5 months for the lesions on the back, 3, 3 and 6 months for the lesions on the forearm and 3, 3, 3 and 6 months for the lesions in the axillae. One individual developed lesions in both axillae (after 3 months), another individual lesions on both forearms (after 3 months), and one individual 1 lesion on the back and 1 on the forearm both appearing after 6 months. The lesions started as multiple pinpoint sized, round, dark papules in linear arrange-

ment. They enlarged and fused, forming a typical papillomatous wart about 2 cm in diameter and 0.5 to 1.0 cm elevated above the normal surrounding skin. The consistency of the lesions varied from soft in moist areas (axillae) to hard and cornified in dry areas. After an average of 6 weeks most of the lesions stopped growing. All of the lesions but 2 were studied histologically. When half of the lesion was excised for biopsy the remainder disappeared spontaneously after 4–5 weeks. The 2 lesions not removed are still present unchanged after an average observation period of 8 months after they developed.

One recipient was specially chosen because he already had extensive papillomatous warts of the beard area. We inoculated him repeatedly with wart and condyloma material. After developing 2 lesions in the axillae following inoculation of condyloma material, the warts of his beard area disappeared spontaneously as well as the remainder of the experimentally produced warts after one half of each was excised for biopsy.

Ten of the 47 inoculated sites were prepared by dermabrasion and cantharidin prior to the inoculation. No warts were observed in any of these areas. Like other workers we were not able to reproduce condyloma lesions by inoculation of condyloma material into the sulcus coronarius penis. Possibly the relatively high percentage of positive inoculations in this study is due to the fact that the original material was taken from a very young "juicy" lesion about 2 weeks old.

Histological studies

Eight biopsy specimens originating from the early experimental lesions (2–6 weeks of age) of 7 individuals were available for serial study after staining with hematoxylin and eosin and by the Feulgen method. We hoped that the examination of very young warts would shed light on the confused question of inclusion bodies which have been differently represented by different authors. Blank *et al* (20) have given a critical analysis of this problem and have concluded from their own studies that the specific inclusion is intranuclear and fulfills all the requirements of newly formed desoxyribose nucleoprotein. The nucleus becomes swollen with virus particles, forcing the chromatin to become marginated at the periphery. These changes are accompanied by ballooning degenerating of the cytoplasm, causing the cell to assume a "bird's eye" appearance. Bunting's (21) findings of virus particles in the nuclei of thinly sectioned papillomas lends weight to Blank's *et al* conclusions which deserve the most careful consideration. It is disquieting, however, that Blank and his associates found intranuclear inclusions in only half of the warts studied. It was a disappointment to us that we could not recognize in any of our 8 early warts any structure that could truly be called an inclusion body. This failure cannot be interpreted to mean that Blank's description of intranuclear inclusions is false. The virus may still be present in the nucleus without regularly provoking the changes which are identifiable as inclusions by standard staining technic.

Comment

We were uniformly frustrated in our efforts to achieve a more successful method of producing warts by special preparation of the skin by dermabrasion and cantharidin blisters. Many factors doubtlessly combine to determine whether a take will occur. Experimental transmission continues to be a capacious affair as is the case with the natural spread of warts clinically. Usually, only one of the inoculated sites of our subjects developed warts, sometimes 2. The conditions for successful inoculation are evidently very delicate. Perhaps this is not so much a question of regional differences in the skin as it is a matter of keeping the virus viable.

Of considerable interest is the uniform regression of the remaining portion of warts that have been excised for biopsy. We may add this species of trauma to innumerable other practices derived from clinical experience and folklore which are recommended for the "cure" of warts. In view of of the mischievous tendency of warts to disappear suddenly, which is usually ascribed to some treatment, and the powerful influence of suggestion in removing warts, we hardly dare to regard as specific the "cure" of a crop of beard warts in one of our subjects in whom warts were produced experimentally. Still, it is interesting that Findlay (3) evidently became immune after 3 successive inoculations. The question of immunity in warts is considered adequately by Blank and Rake (5).

Herpes simplex

In contrast to many other ectodermotropic viruses, the herpes simplex virus can be readily

propagated in laboratory animals. Only few experiments have been carried out on human skin.

Lipschutz (22) in 1921 inoculated material from genital herpes simplex into normal skin areas of the thigh of 31 individuals. Only two were successful (typical grouped vesicles) and 5 weakly positive (vesicles or papules) after an average incubation period of 24–48 hours. Biopsies of the vesicles were positive for herpes; the inoculation of fluid from the experimental blisters into the rabbit cornea induced typical herpetic lesions.

Gruter (23) inoculated herpes material from the rabbit cornea into the cornea of blind human volunteers and reported 9 positive results.

Nicolau and Poincloux (24) used herpes material from the rabbit cornea and inoculated scarified skin areas of the upper arm. Vesicles or papules were noticed in 9 out of 18 inoculations. Herpes material from rabbit brain gave similar results in 4 out of 18 inoculations. Autoinoculations of patients with herpes simplex were positive in 11 out of 13 inoculations.

Teissier (25) performed autoinoculations in patients with herpes simplex and observed herpetic lesions in 13 out of 16 inoculations after 48 hours. He repeated autoinoculations up to seven times in the same individual, the average number of passages achieved in 6 out of 8 cases being 2. Inoculations of herpetic material into normal skin of 10 volunteers were positive in 7 cases.

Findlay (26) described the case of a child who for many years had recurrent attacks in a site on the hand which had been traumatized in infancy. He reviews several other cases of pertinence to the current study since the recurrent attacks occurred on the chronically irritated fingers of hairdressers and dressmakers. Reports such as these suggest that inoculations in prepared skin sites might have a higher chance of success.

Present study

To avoid the risk of a severe primary infection, the selection of subjects was restricted to those who had a positive complement fixation reaction of at least 1:8. The primary infection in all of these was evidently inapparent since none could recall clinical attacks. Normal and prepared skin areas on the forearm were inoculated with virus material from 3 different sources using the multiple pressure technic. The sources were: 1) virus suspension (tissue culture from Wistar Institute, Philadelphia, Pennsylvania); 2) virus suspension (chorioallantoic membrane—Children's Hospital, Philadelphia, Pennsylvania); 3) blister fluid from early herpes labialis lesions. A total of 65 inoculations (42 of them on prepared sites) was performed in 27 individuals. The only occasional reaction observed in the inoculation sites was a small papule, 0.3 cm or less in diameter during the first 3 days after inoculation; vesicles did not develop. These were possibly reactions of hypersensitivity. Blank (personal communication) never succeeded in reproducing herpes simplex experimentally but he, too, saw transient "immune" reactions. This finding is reminiscent of the similar experience with molluscum contagiosum.

The prepared areas showed the same response or no reaction at all; no reaction comparable to "inoculation herpes" could be observed.

Comment

Again, previous workers have had a good deal more success than ourselves in establishing experimental infections. Preparation of the sites availed us nothing. While eczema herpeticum characteristically occurs in dermatitic skin, this is usually of a special kind, chiefly infantile eczema.

Herpes Zoster

Occasional reports of successful transmission of the herpes zoster virus to laboratory animals have not been verified. With one exception, all attempts to produce herpes zoster experimentally in man have been unsuccessful. Most of these experiments had been carried out to establish the relationship between herpes zoster and varicella. Chicken pox has been produced by the inoculation of fluid from herpes zoster vesicles but the reverse experiment has failed uniformly.

Marinescu and Draganescu (27) inoculated contents of zoster vesicles into scarified areas of the upper arm and observed herpes zoster lesions of the chest in 1 out of 15 inoculations after an incubation period of 4 weeks. These experiments could not be verified by other authors. In his attempts to establish the relation between varicella and herpes zoster Kundratitz (28) performed a great number of inoculations. Using material from 6 children with herpes

zoster he inoculated blister fluid into the skin of other children under 6 years of age. In 17 out of 28 inoculations he observed vesicles at the inoculation site after 9–12 days, 2 of them developed generalized varicella later. Inoculations with the same material in adults were unsuccessful. There can be no question of the identity of the herpes zoster and varicella virus.

Lauda and Stohr (29) repeated these experiments and inoculated 55 children with material from 17 different adult patients with herpes zoster. They did not observe any local reactions, however, 3 of the inoculated children developed generalized varicella.

Bruusgard (30) produced 8 cases of varicella (4 localized, 4 generalized) by inoculating 18 children under 5 years of age with zoster material. Experimental inoculations in adults did not give any similar results.

Present study

Blister fluid from early lesions of herpes zoster thoracalis of 2 elderly males was inoculated into scarified normal and prepared skin areas of the arm and thorax. 51 inoculations (30 of them at prepared sites) were carried out in 23 individuals.

In no instance did a take occur, nor were local reactions of any kind observed. The results were hardly surprising in view of the fact that almost all adults here had previous primary infections, apparent or inapparent, of chicken pox which doubtlessly promotes a considerable degree of immunity to clinical reinfection.

DISCUSSION

A pilot study with vaccinia virus seemed to support the hypothesis that freshly regenerated epidermis (presumed to resemble embryonic tissue) would provide a highly suitable substrate for infection with various ectodermotropic viruses. Vaccinia lesions were far more inflammatory and of much greater diameter when the inoculation site was prepared by prior dermabrasion or by raising a cantharidin blister.

Normal and specially prepared symmetrical forearm sites of volunteers were inoculated with the following viruses: molluscum contagiosum, warts (verruca vulgaris and condyloma acuminatum), herpes simplex and herpes zoster. Despite a rather large series of inoculations, not a single success was obtained with molluscum contagiosum, herpes simplex and herpes zoster. No lesions resulted in either prepared or normal skin. Ten of 47 wart inoculations using material from condyloma acuminatum lesions produced warts, but all of these were in normal skin areas. If anything, prior damage to the skin renders it even less susceptible, at least in the case of the wart virus. The hope that clinical infections with the ectodermotropic virus could be produced at will by special preparation of the skin was not fulfilled. With present technics, a high failure rate, up to 100%, is to be anticipated, excluding, of course, the vaccinia or variola viruses. Adult human skin *in vivo* is not a suitable substrate for experimental studies of the pathogenesis or biology of virus infections. It is perfectly clear that simple contact with the virus is not inevitably followed by infection. The reasons for this refractoriness are probably complex. Present knowledge is meager. A partial explanation probably resides in the fact that the subjects in the present study were adults who probably had acquired some degree of specific immunity. Furthermore, these were healthy adult males with probably a high degree of native nonspecific resistance. Previous workers who have had a higher degree of success may have used subjects who were less healthy physically than is the case with contemporary subjects living in the United States where nutritional and hygienic standards are high.

The problem of detecting inapparent infections complicates the study of experimental inoculations. In this connection the long incubation period of warts would seem to represent a period of inapparent infection until something happens after many generations of epidermal cells to bring about manifest clinical changes. The analogous phenomenon in bacteria is lysogeny. Unless the host cell is visibly damaged or altered, there is, as yet, no certain way to recognize whether it is infected or not. This may not become known until its descendents, far removed, suddenly become "diseased". The argument over the existence of inclusion bodies in the common wart clearly relates to this question.

In the field of infectious disease, a new period is dawning in which the all important role of the host is being appreciated, rather than concentrating so intensively on the pathogen. It is particularly in the case of virus infections that brilliant discoveries await the imaginative experimenter who discerns what host factors increase or decrease susceptibility.

SUMMARY

Preparation of the adult skin by dermabrasion or by cantharidin blisters enhances the pathologic response to the vaccinia virus. These technics failed to promote infections with the viruses of herpes simplex, herpes zoster, molluscum contagiosum and warts.

The literature on the inoculation of human skin with the ectodermotropic viruses is reviewed.

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